UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/663,693	09/17/2003	Evgenu Nudler	NUDLER2A	3974

1444 7590 04/13/2007

BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER	
SACKEY, EBENEZER O	
ART UNIT	PAPER NUMBER
1624	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/663,693	NUDLER ET AL.	
	Examiner	Art Unit	
	EBENEZER SACKEY	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *15-20 and 23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14,21,22 and 25-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/16/03 and 12/16/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This is in response to applicant's remarks filed on 01/30/07.

Status of the Claims

Claims 1-27 are pending.

Information Disclosure Statement

Receipt of the Information Disclosure Statement filed on 09/16/03 and 12/18/03 respectively is acknowledged and has been entered into the file. Signed copies of the 1449 are attached herewith.

Response to Restriction

Applicant's election of Group I, claims 1-14, 21-22 and 24-27 in the reply filed on 01/30/07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Thus, claims 15-20 and 23 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a nonelected invention.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14, 21-22 and 24-27 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is

most nearly connected, to make and/or use the invention.

The following phrases are not supported in the specification: In claim 1, "metabolism of nitric oxide" and "perfluorocarbon" page 68, lines 1-2 and page 10; claim 2 "inhibit nitric oxide activity"; claims 3 and 4 "enhance nitric oxide activity"; claim 5 nucleophile; claim 6 "thiol or mixture of thiols"; claim 8 "cardiovascular conditions, HELP syndrome, regulation of blood flow, gastrointestinal disease to alter motility, lung functions autoimmune and immune diseases; resistance to infection, central nervous system conditions, growth hormone disorders, cancer, female reproductive disorders, male reproductive problems, bladder and kidney problems dermatological problems" in claim 21 nitrosative stress; claim 22 regulating perturbations; claim 27 "irradiated with light". The specification fails to adequately teach how to use the invention properly by failing to provide an enabling disclosure regarding the above phrases. Because of the high level of unpredictability associated with chemical or biological systems, a greater amount of evidentiary support is needed in order to fully satisfy the requirement of 35 U.S.C. 112, first paragraph, that applicants provide sufficient guidance as regards "how to use" the invention. For example what is encompassed or contemplated by "metabolism of nitric oxide"? The specification only supports perfluorated emulsions, which provide a source of nitric oxide which may be used for administering nitric oxide to individuals. Clearly, a great deal of experimentation would be required to ascertain what is encompassed by the phrase. It is also not clear what is contemplated by the disorders. Disorders appear in various ways and forms. Currently the diseases or disorders with adequate support are hypertension, asthma, pulmonary hypertension and vasorelaxation. Because of the various pathways and mechanisms associated with other disorders such as for example cancer or

central nervous system conditions, greater amounts of evidentiary support would be required for the instant claims. These expressions consist of various disorders or abnormal conditions with known various pathways. The specification has shown no testing protocol, which may be accepted in the art as being predictive of the utility alleged. Note merely identifying substances as objects for further use testing (speculative utility) is insufficient to provide an enabling disclosure. See Brenner V. Manson, 148 USPQ 689 or In re Kirk, 153 USPQ 48. Additionally, "perfluorocarbons, metabolism of nitric oxide, resistance to infection, cancer, autoimmune" etc., are generic. As defined, the claims embrace a variety of conditions and/or disorders, which are broader than the enabling disclosure.

Applicants need to point out in the specification where there is support for the above phrases. A mere statement does not provide enabling support for such a utility.

In the instant application, the specification is not enabling for the broad class of disorders and conditions encompassed by the invention because of the lack of test data to support all of the above expressions. In view of the unpredictability of chemical systems, and the fact that specific disorders and conditions have not been shown to be effective for the invention, a conclusion of this activity cannot be reached without data for the entire scope of the invention.

In addition, the gap between limited laboratory activity and industrial utility is large enough to warrant thorough and compelling data.

Of course, the inclusion of some inoperative embodiments in a generic claim is not enough in itself to render the claim unpatentable. However, when the number of inoperative embodiments becomes significant, or when the likelihood is high that a significant number of the embodiments are inoperative,

one of ordinary skill must resort to undue experimentation to practice the claimed invention, and at this point the generic may properly be found to be unpatentable. See Atlas Powder Co. V. E.I. Dupont de Nemours, 750 F .2d 1569, 1576 (Fed. Cir. 1984).

"In cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty in their performance characteristics predicted by resort to know scientific law. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of factors involved." Amgen, Inc. V. Chugai Pharmaceutical Co. Lts., 13 USPQ .2d 1737, 1775 (1980), citing In re Fisher, 527 F .2d 833, 839 (CCPA 1970). The Amgen decision, Id. At 1776, went on to point out that, while 50 to 80 analogs had been tested in vitro and exhibited activity varying over several orders of magnitude, this was not sufficient to conclude that the same analogs would have comparable biological activity. The case of non-enablement was therefore found to be even stronger against the remaining analogs encompassed by the implicated claim, for which in vitro data had been furnished. After extensive testimony, the claim was held invalid for the failure to satisfy the enablement requirement of sec. 112.

The present rejection is believed to be consistent with the aforementioned decisions, as well as the decision in In re Marzocchi, 169 USPQ 367, 369 (1971) in which the court stated that:

"As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the

subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. Assuming that sufficient reason for such doubt does exist, a rejection for failure to teach how to make and/or use will be proper on that basis, such a rejection can be overcome by suitable proof indicating that the teaching contained in the specification is truly enabling."

By suggesting that specific disorders or conditions may be required to show that the instantly claimed invention satisfies that enablement requirement, the Examiner does not wish to determine the lack of inhibitory activity of the claimed method of using the composition, but rather to determine if specific disorders or conditions benefit have been attained.

The specification is devoid of disclosure, which would direct the skilled artisan to all disorders or conditions embraced by the above claims. It is suggested that specific conditions or disorders be disclosed. Such would appear to obviate the rejection. However, applicants should note that the insertion of disorders or conditions etc., into the specification or claims could raise the issue of new matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-14, 21-22 and 24-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. The use of the word "perfluorocarbon" is of indeterminate scope because the word is very generic. Moreover, perfluorocarbons are compounds derived form hydrocarbons by replacement of hydrogen atoms with fluorine atoms. The length of the perfluorated carbon chain determines what the physical properties and the utility of the perfluorocarbon will be, e.g., perfluoro-propane is utilized during eye surgery. Additionally, metabolizing nitric oxide is not considered a disease.

2. The plethora of intended uses present in the claims renders the intended "amount" ambiguous since it is not conceivable that the dosage regimens for uses as varied as cardiovascular disease vs. autoimmune disease vs. impotence vs. osteoporosis would all be the same and there is nothing in the specification pointing to a particular regimen for the many uses recited. It is suggested that the uses be deleted since only one use in needed to support such a claim for compliance with 35 U.S.C. 112 and 101. See the last paragraph of MPEP 2164.01(c), November 2005 edition.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 8-14 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Garfield et al., (U.S.Patent number 5,869,539).

Applicants claim a method for controlling metabolism of nitric oxide comprising the administration of an effective amount of a perfluorocarbon composition.

Claim 1 is drawn to a method for controlling nitric oxide metabolism by administering to an animal in need thereof an effective amount of a perfluorocarbon. Claims 8-14 limit claim 1 by specifying the animal to receive the perfluorocarbon must be suffering from a disease or condition. Claim 8 is drawn to a plethora of conditions and diseases. Claims 9-14 further limit the condition or disease the animal administered the perfluorocarbon must have. Claim 26 is drawn to treating leukemia in a patient by administering a perfluorocarbon.

The Garfield et al. patent anticipates claim 1 where deoxygenated perfluorocarbon emulsions containing nitric oxide are administered to mammals, see column 8, lines 54-65. The conditions Garfield et al. assert the perfluorocarbon emulsion will control or affect NO are in column 9, line 53 through column 10, line 29. The conditions and/or diseases disclosed include cardiovascular conditions, regulation of vascular conductance, regulation of blood flow and pressure, myocardial ischemia, topical hair loss, eczema, psoriasis, renal arterial stenosis, blood clotting, cancer and lung functions. These conditions are seen to anticipate the administration of a perfluorocarbon to an animal in need thereof, since the conditions and diseases of the Garfield patent would be inherently treated upon the administration of a perfluorocarbon compound as instantly claimed.

Claim Rejections - 35 U.S.C. § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-4, 8-14, 21-22 and 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garfield et al., (U.S.Patent number 5,869,539).

Applicants claim a method for controlling metabolism of nitric oxide comprising the administration of an effective amount of a perfluorocarbon composition

Determination of the scope and content of the prior art (MPEP §2141.01)

Garfield et al., teach the use of perfluorocarbon emulsion for treating various disease states. See the entire reference especially column 8, lines 54-67, and column 9 lines 1-27. Note the various treatable diseases with the emulsion in column 9, lines 55-67 and column 10 lines 1-29, note cardiovascular diseases, hypertension, toxemia, autoimmune diseases, Alzheimer's, penile erection, blood clotting, enhancing ischemic preconditioning, restenosis, preeclampsia etc. These are all diseases currently claimed (claims 8-14). Also note the treatment of cancer (leukemia) and resistance to infection, which is inclusive of treating viral diseases (claim 25). With respect to claim 27, the reference is silent on the use of the emulsion to irradiate a patient. However, since the reference emulsion is similar to the currently claimed emulsion, it could be inferred that such properties are inherent in the reference emulsion.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The instant invention differ from the prior art in that specific ratios of the emulsion administered to patients i.e., claims 2-4, however, the claimed ratios are an obvious modification available to one of ordinary skill in the art. They are merely optimization of variables, which are not patentable absent unexpected result due to these variables, and hence are a difference in kind, and not merely in degree from that of '570'. *In re Aller,* 105 USPQ 233, (1955). Also see *In re Boesch*, 205 USPQ, 215, (1980). The application claims a method of treating various disease states by controlling the metabolism of nitric oxide comprising the administration of a perfluorocarbon. The application method and the reference

method are essentially the same and will treat essentially the same diseases.

Finding of prima facie obviousness---rational and motivation (MPEP §2142-2143)

Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time of this invention since Garfield et al., discloses that perfluorocarbon emulsions are useful for treating various ailments. Therefore, one in possession of Garfield et al., is in possession of the instant method absent a showing of unexpected results or properties.

Hence, one of ordinary skill in the art would be motivated to treat humans with a known perfluorocarbon emulsion with the expectation that the resulting treatment would be successful in humans.

Thus, the instantly claimed method would therefore have been suggested to one of ordinary skill in the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to E. Sackey whose telephone number is (571) 272-0704. The examiner can normally be reached on Monday-Friday from 7:30 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached on (571) 272-0661. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

EOS
March 31, 2007

James O. Wilson

Supervisory Patent Examiner
Art Unit 1624, Group 1600
Technology Center 1